The Perioperative Stress Response

ONE REASON SURGICAL PATIENTS ARE DIFFERENT FROM MEDICAL PATIENTS

Objectives

Outline the surgical stress response elicited by the tissue injury of surgery.

Outline strategies to prevent stress response induced complications.

Medical versus Surgical Patients

- There is a difference in medical patients and surgical patients. Sometimes healthy patients are having surgery and sometimes we have patients with a lot of comorbid medical conditions having surgery.

- Surgical patients experience a stress response which is a reaction of the human body to the noxious stimuli of the surgery.
Stress Response and Existing Health

- Physiological responses elicited in the body with surgical stress include sympathetic nervous system, endocrine system and immunological responses.

- The physiological responses elicited by the stress response can interact with baseline medical conditions to create complications.

Study of the Stress Response

- The study of the body’s stress response began with studies of patients’ with accidental injuries.

- Curiosity spread to study tissue injury during surgical procedures.

- It is important to know that the degree of surgical stress that is exerted on the patient is proportional to the tissue injury. The level of tissue damage determines the level of stress response.

Little Tissue Injury-Little Stress Response
Big Tissue Injury-Big Stress Response

Surgical Procedure

Critical Assessments by PACU Nurses

• PACU nurses are responsible for assessing our patients to identify and predict if the physiological changes elicited by the stress response of surgery will interact with any baseline medical problems.

• Critical assessment skills and knowledge of the stress response will prevent complications in complex patients.

PACU Nurses *Can* Make a Difference
What is Stress?

STRESS

Stress is...............

Stress is...............

"STRESSED" is "DESSERTS" spelled backwards
Surgery is Stressful

Some Other Causes of Stress
- Physical trauma
- Pain
- Fear
- Prolonged exposure to cold
- Infection
- Shock
- Decreased oxygen supply
- Prolonged heavy exercise

Stress Response
- The stress response includes the “fight or flight” response in which we can all picture a man running away from a growling tiger.
- A surgical procedure elicits a sympathetic nervous system response from the body.
- Sympathetic response is “fight or flight”
- Parasympathetic response if “rest and digest”
Think of a Moment of Panic

Central Nervous System Responses

Consider the Rationale for the Stress Response

The rationale for the body’s response is:
- Fight – the ability to defend yourself from a threat
- Flight – the ability to run away FAST
- Pupil dilation – increased visual acuity
- Secretion of epinephrine and norepinephrine – increased heart rate, BP, and cardiac output
- Relaxation of the bronchi – increased ventilatory capacity
- Analgesia – the ability to have relief from the pain of tissue damage
- Increased coagulability - to limit blood loss
- Mechanisms to retain Na and water – maintain fluid volume and cardiovascular homeostasis
- Peripheral vasoconstriction - support the BP and shunt blood to vital organs
- Stimulation of glucose release by the liver - to provide energy sources
Why Do We Care?

- The reason that this stress response of the body is so important to us in PACU is because the physiological changes elicited by the stress response can interact with baseline medical conditions to create complications.

- We need to intervene as necessary to blunt the stress response and thus prevent complications.

- PACU nurses are in the unique position to identify and treat signs and symptoms of the stress response before they result in a complication.

PACU Nurses Predict the Responses to Stress

PACU Nurses Prevent Complications
The Nurses Critical Role

- The perioperative staff has a responsibility to think ahead and predict what stress responses can be prevented or blunted and intervene as necessary.

- PACU nurses are in the unique position to identify and treat signs and symptoms of the stress response before they result in a complication.

Many Factors Affect the Stress of Surgery

- Severity of the tissue injury
- Pre-existing pathology (past medical history)
- Genetic predisposition
- Surgeon expertise
- Experience of the surgical team
- Anesthesia management
- Type of surgical procedure
- Timing and length of the surgical procedure
- Pain relief
- Anxiety
- Thermoregulation
Hypothalamic Pituitary Adrenal Axis

Stress Stimulates the HPA Axis

Hypothalamic Releasing Factor Stimulates the Pituitary Gland
Anterior Pituitary Releases ACTH

The hypothalamic releasing factor stimulates the anterior pituitary to synthesize:
- Adrenocorticotropic hormone (ACTH)
- Growth hormone (GH)
- Thyroid stimulating hormone (TSH)

ACTH stimulates release of cortisol from the adrenal cortex.
- Cortisol is a glucocorticoid
- Cortisol is released to increase blood glucose, aid in fat, protein, and carbohydrate metabolism
- Cortisol is the body’s natural anti-inflammatory agent

Anterior Pituitary Releases Growth Hormone

- GH has an anti-insulin effect by inhibiting glucose uptake and use by cells. This takes place in order to save the glucose for a situation of glucose scarcity.
- GH stimulates protein synthesis and inhibits protein breakdown
- GH promotes lypolysis which is the breakdown of triglycerides into fatty acids and glycerol
- Beta endorphins increase in circulation after surgery due to increased pituitary hormone secretion

Posterior Pituitary Secretes Vasopressin

- The posterior pituitary secretes vasopressin: a potent vasoconstrictor and anti-diuretic hormone.
- Vasopressin promotes water retention and urine concentration, thus causing the kidneys to save fluid and decrease urine output.
- Usually the urine output is limited for 3-5 days and is followed by a period of diuresis.
- Also, the kidney itself secretes renin and stimulates angiotensin II which in turn stimulates release of aldosterone from the adrenal cortex. This causes sodium and water reabsorption in the kidney.
Adrenal Glands are Stimulated

Adrenal Cortex

Cortisol is rapidly secreted from the adrenal cortex following the start of surgery. The cortisol secretion is released in proportion to the degree of the injury.

Increased cortisol usually inhibits further secretion of ACTH, but this control feedback mechanism is ineffective after surgery. Both ACTH and cortisol remain high.

Cortisol is nature’s steroid. Cortisol has glucocorticoid effects as well as anti-inflammatory effects.

Increase aldosterone secretion which leads to increased sodium and water reabsorption.

The Cortisol Response Can be Modified by Anesthetic Intervention
Adrenal Cortex

- Cortisol promotes protein breakdown and gluconeogenesis in the liver.
- Cortisol will inhibit glucose use by cells in order to keep blood glucose concentrations high. It promotes breakdown of triglycerides to glycerol and fatty acids. This provides and conserves energy sources.
- Cortisol inhibits accumulation of macrophages and neutrophils into areas of inflammation and can interfere with synthesis of inflammatory mediators (prostaglandins).

Adrenal Medulla Secretes Catecholamines

- Responsible for the secretion of catecholamines.
- The adrenal medulla is located at the center of the adrenal gland surrounded by the adrenal cortex.
- Consists of cells that secrete epinephrine and norepinephrine.
- Adrenal medullary cells are modified postganglionic neurons but rather than releasing a neurotransmitter, the cells secrete hormones.

Hypothalamic Pituitary Adrenal Axis

- Hypothalamus
  - Anterior Pituitary (ACTH)
  - Posterior Pituitary (vasopressin)
- Adrenal Cortex (glucocorticoids)
- Adrenal Medulla (catecholamines)
Insulin Secretion is Decreased with Surgery

Pancreas

Insulin is synthesized and secreted by the B cells of the pancreas. Insulin promotes glucose uptake into muscle and adipose tissue and conversion of glucose into glycogen and triglycerides.

Insulin secretion is decreased after induction. Insulin secretion fails to match the catabolic, hyperglycemic response thus blood glucose levels remain high.

Poor glycemic control with blood glucose greater than 200 is associated with impaired wound healing and wound infections.

Thyroid Hormones Can Potentiate Catecholamines
Thyroid

- Thyroid hormones stimulate the oxygen consumption of most of the metabolically active tissues of the body.
- There is a close association between the activity of thyroid hormones and catecholamines.
- Epinephrine and norepinephrine increase the metabolic rate and stimulate the nervous system.
- Thyroid hormones increase the number and affinity of B-adrenergic receptors in the heart and increase the sensitivity of the heart to the actions of catecholamines.

Pathway From Injury to the Brain

- Surgery is one of the most potent activators of ACTH and cortisol.
- Within minutes of surgical start, both increase.
- The afferent neuronal impulses at the site of injury send signals through the sensory nerve roots, through the dorsal root of the spinal cord, and travel up the spinal cord to the medulla which activates the hypothalamus. Thus beginning the cascade of stress hormones.

Afferent Neuronal Pathway to the Brain
Cytokines are produced from activated leucocytes, fibrinoblasts and endothelial cells as an early response to tissue injury. Cytokines are proteins. (interleukins or interferons) Cytokines have a major role in the inflammatory response to tissue injury. After surgery, cytokines mediate and maintain the inflammatory response. First, Interleukin 1 (IL1) and tumor necrosis factor alpha (TNF) are released from activated macrophages and monocytes in the damaged tissues. This in turn stimulates production and release of more cytokines interleukin 6 (IL6).

Cytokine production reflects the degree of tissue trauma. For example, it is low with a laparoscopic procedure and much higher with joint replacement of colorectal procedure. Laparoscopic surgery causes less tissue damage than open surgery, so the increase in concentrations of biochemical markers of inflammation (IL6 and CRP) are not as great.
Cytokines

- Cytokines are the most important group of inflammatory mediators as they regulate alterations in hemodynamics.
- Cytokines regulate functions of activated cells in order to maintain homeostasis.
- Cytokines are produced by diverse cell types at the site of injury and by systemic immune cells.
- Their rapid appearance after injury reflects active action by the injured or stimulated cell.
- Cytokines can regulate the production and activity of other cytokines which may either augment or attenuate the inflammatory response.

C-reactive Protein

- The liver produces proteins that act as inflammatory mediators.
- These proteins from the liver include C-reactive protein (CRP) and fibrinogen.
- Increase in serum CRP follows the change in IL-6.
C-Reactive Protein

Cytokines Reflect Degree of Tissue Damage

- Cytokines IL1 and IL6 stimulate secretion of ACTH from pituitary cells.
- After surgery, cytokines may augment pituitary ACTH secretion and subsequently further increase release of cortisol.
- Anesthesia has little effect on the cytokine response to surgery because it cannot influence the tissue trauma.
- Regional anesthesia inhibits the neuro-endocrine response but has no effect on cytokine production.

Cardiovascular Changes with Surgery
Cardiovascular Changes with Surgery

- Catacholamine mediated increased heart rate
- Increased risk of tachyarrythmias (VT, a-fib)
- Increased myocardial contractility
- Increased myocardial oxygen consumption
- Increased BP
- Risk of myocardial ischemia

Cardiovascular Changes with Hypothermia

- Even mild hypothermia activates thermoreceptors which are conveyed to the hypothalamus.
- The hypothalamus initiates appropriate measures to restore normothermia.
- Primary defenses against cold are arteriovenous shunt, vasoconstriction and shivering.
- Shivering can be a serious complication if the patient has a compromised cardiovascular system due to the increased myocardial oxygen demand.
Complications Related to Hypothermia

- Vasoconstriction works by decreasing cutaneous heat loss and restricting metabolic heat to the core.
- Hypothermia will increase risk of tissue ischemia and wound failure.
- Hypercoagulability leading to thrombotic events (PE, DVT)
- Systemic inflammatory response

Renal and Electrolyte Changes with Surgery

- Vasopressin is secreted from the Posterior Pituitary to promote water retention and urine concentration.
- Renin is secreted from the kidney itself and stimulates angiotensin II which stimulates the release of aldosterone from the adrenal cortex so that water and sodium will be reabsorbed.
- Complications can include CHF and hyponatremia. SIADH
Renal and Electrolyte Changes With Surgery

- Na retention (lasts 3-5 days)
- Decreased free water clearance (lasts 5-7 days)
- Decreased K+
- Decreased Mg++
- Leukocyte levels increase immediately postoperatively and stay elevated for about 48 hours

Renal Considerations

- Be aware of low cardiac output states and renal perfusion.
- Take into account if the patient has had contrast dye.
- Be aware of nephrotoxic medications (vancomycin, gentamycin, tobramycin, ciprofloxacin, levoquin, NSAIDS, tetracycline, rifampin)

Metabolic Changes with Surgery

- Increased blood glucose
- Increased protein catabolism
- Protein and fat breakdown in the periphery
- Increased lactic acid production from glucose in the periphery.
- Augmented hepatic glucose synthesis.
Pulmonary Changes with Surgery

- Formation of atelectasis
- Changes in the diaphragm position and movement
- Decreased mucociliary clearance of secretions
- Increase in alveolar-capillary permeability
- Respiratory depression and thus hypoventilation from opiates and inhalational anesthetic agents
- Reversing versed or opioids emphasizes treatment of increasing patient’s alertness more than reversing respiratory depression

Pulmonary Changes with Surgery

- Indirect manipulation of the lungs during surgery
- Supine or trendelenburg positioning in the OR
- Mechanical ventilation
- Paralytic agents (even when fully reversed)
- Increased pulmonary vascular permeability can result in decreased gas exchange and pulmonary edema.
- Decreased cough effort due to pain.
Temperature Changes with Surgery

- Hypothermia is associated with adverse clinical complications such as myocardial ischemia, impaired coagulation, reduced resistance to infections, delayed wound healing, prolonged emergence, increased recovery time and cost.
- Even mild hypothermia can trigger sympathetically mediated hypertension due to norepinephrine.
- Cortisol increases have a significant role in the response to cold stresses and are associated with immune inhibition.
- When the core temperature is low the patient develops a coagulopathy and decreased platelet function.

Are You Sleeping?
Strategies

It’s time to go through strategies that we can do to prevent stress response induced complications.

Attenuate the Stress Response

Strategies to Attenuate the Stress Response

- Prevent hypothermia
- Regional anesthesia
- Peripheral nerve blocks
- Wound infiltration with local anesthetics
- Multimodal pain medication
- Opioids
- NSAID’s
- Locals
- Dexamethasone
- Beta blockers
- Benzodiazepines
- Alpha 2 agonists
Prevent Complications in the PACU

- Anesthetics suppress many elements of the stress response
- Most problems occur post-operatively.
- Knowledge of the stress response physiology can help guide our care postoperatively.

Prevention of Hypothermia

- Forced air warming blunts the sympathetic nervous system response.
- Increased levels of catecholamines exacerbates vasoconstriction and reduces tissue PO2.
- The normal response to hypothermia includes activation of the sympathetic nervous system.
- Even a small change in core temperature are associated with thermoregulatory vasoconstriction.
- Shivering causes increased O2 demand

Maintain Warmth
Warm and Safe

Hypothermia Effects on the Body

- Increases the risk of serious myocardial outcomes
- Increases risk of VT and other arrhythmias
- Increases the risk of surgical wound infection
- Increases blood loss and transfusion requirements
- Prolongs recovery and hospitalization
- Exposes patient to increased surgical stress
- Potentiates catecholamine response
- Prolongs anesthetic and paralytic agents
- Decreases leukocyte functioning

Thermoregulation

- Anesthetics inhibit thermoregulatory control.

- After induction the circulating volume redistributes decreasing the core body temperature.

- Vasodilation causes heat to move from the core to periphery.
Regional Anesthesia

- Regional anesthetics using local anesthetics can reduce the classic pituitary, adrenocortical, and sympathetic responses to surgery.
- Extensive epidural anesthetic will abolish the cortisol and glucose responses to surgery.
- The combination of local anesthetic and opioid given epidurally results in synergistic analgesia that is superior to either given alone.

Neural blockade techniques have been developed and provide attenuation of the stress response thereby reducing postoperative organ dysfunction and allowing early recovery.
- Regionals do not modify inflammatory or immunological responses to surgery.
- Regional anesthetic blocks afferent signals to the CNS and efferent autonomic neuronal pathways to the liver and adrenal medulla.

Epidural Anesthesia

[Image of epidural anesthesia procedure]
Benefits of Epidural Anesthesia

- Superior pain relief
- Less sedation
- Decreased cardiac complications
- Decreased pulmonary complications
- Decreased neuro-endocrine stress response
- Lower incidence of embolic events (DVT, PE)
- Earlier return of bowel function
- Prevention of chronic pain syndromes
- Decreased length of stay

Regional Anesthesia is Superior

- The superior effects of regional anesthetic techniques are manifest by improved pulmonary function, decreased cardiovascular demands, reduced ileus and improved pain relief.
- In addition, decreased incidence of DVT with regional blocks.
- Also, studies have shown reduction in blood loss in THR patients with regional due to lower arterial and venous pressure.

Tissue Damage of Surgery is Painful
Understanding Pain

- Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage.
- Pain is what the experiencing person says that it is.
- There can be neuropathic pain from manipulation of nerves during surgery.
- There will be inflammatory pain from the tissue damage at the surgical site.
- There can be cramping pain from prostaglandin release.

Pain

- Pain from tissue damage of surgery
- Neuropathic pain from the nervous system
- Inflammatory pain
- Pain from stretching or distension
- Pain from degenerative changes
- Pain from reduced oxygen supply of tissues

Pain Hurts
Pain has Adverse Outcomes

Wound Infiltration
- Infiltration with local anesthetics not only provides analgesia but also appears to reduce the local inflammatory response to surgery.
- Local anesthetics act on sodium channels to inhibit transmission of impulses along the peripheral nerves but all excitable tissues can be affected.

Local Anesthetics
- Local anesthetics cause a reversible numbness.
- Locals act on sodium channels to inhibit transmission of impulses along peripheral nerves.
- The local anesthetic acts by inhibiting the influx of sodium through ion channels in the neuron cell membrane. When the influx of sodium cannot arise then conduction is inhibited.
On Q Pump

Peripheral Nerve Blocks

- Interscalene blocks for shoulder surgery
- Supra-clavicular blocks for shoulder surgery
- Axillary block for hand and wrist surgery
- Femoral blocks for lower extremity surgery
- Nerve blocks done at the site of surgery by the surgeon

Multimodal Pain Medication
Pre-emptive Pain Medication

Pre-emptive analgesia (analgesia that is started prior to the noxious stimulus) is a logical approach to preventing pain induced changes in nociceptive processing.
Locals, blocks and regionals.
Prevention of chronic pain syndromes.

Multimodal Pain Control

Acetaminophen
Opioids: (dilaudid, morphine, fentanyl)
Non-steroidal anti-inflammatory agents: (celebrex, toradol, motrin)
Anticonvulsant medications: (neurontin, lyrica)
Benzodiazepines: (versed, valium, ativan, xanax)
Anti-emetics when needed

Chronic Pain Prevention

Post-op pain should be vigorously treated as it may amplify the surgical stress responses and organ dysfunction and prolong recovery.
Chronic pain is likely caused by iatrogenic nerve damage.
Aggressive early therapy for postop pain and better management of intra-operative pain are likely the most effective interventions for preventing chronic pain.
Acute post-operative pain can be followed by persistent pain in 10-50% of patients even after common operations. (hernia repair, mastectomy, thoracotomy, amputation)
Non-Medication Pain Relief

- Position for comfort
- Assess skin and pressure points
- Support arms with blankets or pillows
- Elevation of operative extremity
- Ice therapy
- Gatch the knees to help back and abdominal pain
- Invite family in for a “quick hello”
- Cough pillow for abdominal procedures
- Warm blankets

Pain Has Adverse Outcomes

Adverse Outcomes of Pain

- Cardiovascular stress
- Increased blood clotting
- Tissue breakdown
- Immune dysfunction
- Chronic pain syndromes
- Delayed bowel function
- Fluid retention
- Pulmonary dysfunction
- Increased metabolic rate
- Autonomic hyperactivity
Opioids

- Opioids suppress hypothalamic and pituitary hormone secretion.
- Opioids can decrease the cortisol response.
- Not all types of pain are equally sensitive to opioids.
- PCA is preferred because patients that feel in control experience less pain.

Side Effects of Opioids

- Respiratory depression
- Vasodilation
- Hypotension
- Bradycardia
- Delayed gastric emptying
- Reduced peristalsis
- Constipation
- Nausea and vomiting
- Puritis, histamine release

NSAIDS

They improve pain levels without respiratory depression and sedation.
Works as anti-inflammatory and reduces the production of inflammatory prostaglandins.
NSAIDs are synergistic with opioid PCA’s

Toradol allows reduced pain with movement, reduced bladder spasms, 40% less opioids used, earlier recovery of GI function.
**NSAID Contraindications**

- GI bleeding, ulcer disease
- Operative site bleeding/oozing
- Renal Insufficiency or Failure
- Low cardiac output states (low EF)
- Thrombocytopenia, coagulation defects
- Plastic surgery patients
- Aspirin induced asthma
- Bone healing
- Hypersensitivity reactions

**Decadron Administration**

- Preoperative single dose dexamethasone (8mg) significantly reduces the pain scores, PONV and antiemetic requirements while improving the respiratory function in the postoperative period. (Sistla, Rajesh, Sadasivan, Kundra)

**Beta Blocker Therapy**

- Beta blockers are effective in treatment of postoperative SVT
- Increased norepinephrine plasma concentrations will increase the MAP
- Postoperative HTN is associated with elevated plasma catecholamines.
- Sympathetic nervous system events include increased heart rate, increased BP, MI and hypercoagulability
**Benzodiazepines**
- Attenuates the cortisol response
- Helps the patient be less anxious
- Provides sedation and amnesia for surgery
- Benzodiazepines are skeletal muscle relaxants

**Etomidate**
- Etomidate interferes with production of steroids in the adrenal cortex by reversible inhibition of enzymes. The synthesis of aldosterone and cortisol is blocked.
- Cardiovascular stability.
- Glucose levels more stable

**Clonadine-Alpha 2 Agonist**
- Clonadine stimulates the alpha 2 receptors in the brain causing decreased cardiac output, decreased peripheral vascular resistance and decreased blood pressure.
- Clonadine reduces the sympatho-adrenal and CV responses caused by the noxious surgical stimuli.
- Blunts the sympathetic nervous system.
- The alpha 2 agonists directly modulate catecholamines.
- Clonadine has a specificity toward pre-synaptic alpha-2 receptors in the vasomotor center and inhibits the release of norepinephrine.
Alpha 2 Agonists

• Potentiation of anesthetic agents
• Decreases analgesic requirement
• Intensifies conduction block of local anesthetics
• Local vasoconstriction
• Blocks A delta and C fibers conduction
• Release of endogenous enkephalins
• Blunts the sympathetic nervous system response

Study Comparing Lap and Open Choley

• This study was conducted to compare the metabolic and inflammatory responses after laparoscopic and open cholecystectomy in terms of serum glucose, cortisol and C-reactive protein.
• It was found that metabolic responses like serum cortisol and glucose were significantly higher after an open procedure.
• Similarly, inflammatory response indicator C-reactive protein was raised significantly higher in the open versus the lap choley group.
• The study included 100 patients age 20-60, with 78 female and 22 males.

Serum Cortisol

<table>
<thead>
<tr>
<th>TIMING</th>
<th>LAPAROSCOPY</th>
<th>OPEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>0.44±0.05</td>
<td>0.42±0.04</td>
</tr>
<tr>
<td>6 hours post-op</td>
<td>0.57±0.03</td>
<td>1.4±0.26</td>
</tr>
<tr>
<td>48 hours post-op</td>
<td>0.57±0.05</td>
<td>0.97±0.07</td>
</tr>
</tbody>
</table>
Serum Glucose

<table>
<thead>
<tr>
<th>TIMING</th>
<th>LAPAROSCOPY</th>
<th>OPEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>99.27±8.76</td>
<td>104.56±10.47</td>
</tr>
<tr>
<td>6 hours post</td>
<td>114.43±11.85</td>
<td>128.26±11.59</td>
</tr>
<tr>
<td>48 hours post</td>
<td>106.93±11.27</td>
<td>117.62±11.13</td>
</tr>
</tbody>
</table>

C-Reactive Protein

<table>
<thead>
<tr>
<th>PROCEDURE</th>
<th>CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lap (N=58)</td>
<td>15.35±3.99</td>
</tr>
<tr>
<td>Open (N=42)</td>
<td>41.67±10.57</td>
</tr>
</tbody>
</table>

References

- Breslow, Michael. The perioperative Stress Response
- Anees, Islam, Saifullah, Hussain. Comparison of Metabolic and Inflammatory Stress Response after Laparoscopic and Open Cholecystectomy. Internet Scientific Publications Vol 22 Number 2
References (continued)


---

Pink Glove Dance

http://www.youtube.com/watch?feature=player_detailpage&v=OREfV6-mLw

---

Thank you for your attention!